REMARKS

Claims 1-11 are pending in the present application. By this Amendment, Applicant has amended claims 1 and 10 for clarity. This Amendment does not introduce any new matter and thus its entry is respectfully requested. Upon entry of the present Amendment, claims 1-11, as amended, will be pending and under examination.

December 15, 2005 Office Action

Claim Rejections Under 35 U.S.C. § 112

In the December 15, 2005 Office Action, claims 1-11 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite. The Office Action asserted that it is not understood what is meant by the word "substantially" in claims 1 and 10 in the recitations "substantially enhancing antineoplastic effects" and "substantially reducing toxic side effects." The position expressed in the Office Action is that these recitations are not defined in the specification. The Office Action also posed the questions "Does it mean that a synergistic effect is seen using the method of using the combination of 5-FU and the methylol transfer agent?" and "Does it mean, e.g., that the patient loses less hair, has fewer mouth sores, is less tired[?]" The Office Action stated that it is not clear (and not described in the specification) which side effects are reduced or how the reduction is measured.

The Office Action also stated that in claim 1, line 2, the term "5-FU" is indefinite. The Office Action asserted that the first time an abbreviation is used in a claim, it should be preceded by the term for which it is an abbreviation.

The Office Action stated that in claim 10, it is not clear that a combination is being

claimed, and suggested that amending the claim to recite "A combination comprising 5-Fluorouracil (5-FU) and a methylol transfer agent..." would overcome this aspect of the rejection.

In response, without conceding the correctness of the positions taken in the Office Action, but to expedite allowance of the application, Applicants have amended claim 1 to include the term "5-Fluorouracil" before the first occurrence of "5-FU." Applicants also have amended claim 10 in the manner suggested in the Office Action.

With respect to the assertion set forth in the Office Action that the recitation of "substantially" is indefinite, Applicants respectfully traverse. Applicant's claimed invention is directed to, *inter alia*, a method of inhibiting tumor growth in a cancer patient comprising administering to said patient a combination therapy comprising effective amounts of 5-Fluorouracil (5-FU) and a methylol transfer agent, said methylol transfer agent being capable of substantially enhancing antineoplastic effects of said 5-FU, substantially reducing toxic side effects of said 5-FU, or a combination thereof, wherein said methylol transfer agent has a substantial effect on activity of said 5-FU, said substantial effect being selected from the group consisting of substantially enhancing antineoplastic effects of said 5-FU, substantially reducing toxic side effects of said 5-FU, and a combination thereof.

Applicants first point out that the specification provides an example showing a significant decrease in proliferation of colo-rectal tumor cells following treatment by taurolidine (a metholyl transfer agent) and 5-FU, and indicating that there was an increase in LDH release, which correlated with inhibited tumor proliferation. Moreover, taurolidine was found to augment (i.e., enhance) the effects of given doses of 5-FU. Furthermore, U.S. Pat. No. 6,479,481, to which the present application claims priority as a continuation-in-part, discloses the use of Taurolidine and/or Taurultam with antineoplastic agents for the treatment of cancer,

and the concomitant reduction of side effects upon such use. (See especially, Example 2). These benefits include, for example, "avoid[ing] or reduc[ing] side effects such as nausea, vomiting, diarrhea, etc., induced by use of neoplastic medicaments." The '481 patent also teaches synergistic effects of such combinations, stating that "[t]he dosage of these antineoplastic medicaments can be reduced by up to half or more and still increase the overall response rate (disease stabilization rate) by synergistic effects," and that the reduction is substantial enough to avoid or reduce radiotherapy (and thus its strong side effects) in many cases. (Column 9, lines 19-24). Moreover, in addition to the specific disclosure that the Office Action has acknowledged, i.e., use of a combination of Taurolidine and/or Taurultam with 5-FU after surgical resection of glioblastoma, there is also a Table shown at column 10 which indicates that 5-FU is particularly suitable for combination with Taurolidine/taurultam to achieve the synergistic results described in the Example. The specification therefore teaches that the claimed combination provides an unexpected synergistic effect that results in significant, identifiable increases in anti-cancer effectiveness and significant, identifiable reductions in the common side effects typically induced by neoplastic agents. One of ordinary skill in the art would therefore readily recognize what both "substantial" reduction of side effects and "substantial" enhancement of anti-neoplastic effects entail in the treatment of tumors.

With these teachings in mind, Applicants direct attention to MPEP §2173.05(c), which provides that the term "substantially" is not indefinite if one of ordinary skill in the art would recognize its meaning from the general guidelines provided in the specification. As indicated above, the guidelines provided in the specification, including the disclosure set forth in the parent cases, would clearly be sufficient to guide one of ordinary skill to this recognition. Accordingly, Applicants respectfully request that the rejection of the claims under 35 U.S.C.

§112, second paragraph be withdrawn.

Claim Rejections Under 35 U.S.C. §103

Claims 1-11 were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Carter, in view of WO 92/00743.

According to the Office Action, Carter discloses that 5-FU is useful to treat the instantly recited cancers. The Office Action acknowledges that Carter does not disclose a method of using taurolidine or taurultam to treat cancer. The Office Action asserts, however, that WO 92/00743 (pages 1-3) does disclose a method of using taurolidine and taurultam to treat cancer. The position stated in the Office Action is:

> "'[I]t is *prima facie* obvious to combine two compositions each of which is taught by the prior art to be useful for the same purpose, in order to form a third composition and use it in a method for the very same purpose...[T]he idea of combining them flows logically from their having been individually taught in the prior art.' *In re Kerkhoven* 105 USPQ 1069."

"Therefore," the Office Action continues, "in the absence of a showing of unexpected results, it would be obvious to one of ordinary skill to combine 5-FU and taurolidine or taurultam to yield the instant composition and use it in a method to treat cancer, since each is individually taught in the prior art to be useful to treat cancer."

Claims 1-11 also were rejected under 35 U.S.C. §103(a) as allegedly being unpatentable over Carter, in view of US 6,303,596. The Office Action reiterated the rationale set forth above, again asserting that Carter discloses that 5-FU is useful to treat the instantly recited cancers, but does not disclose a method of using taurolidine or taurultam to treat cancer. However, according to the Office Action, U.S. Pat. No. 6,303,596 (abstract and claims) does disclose a method of using

taurolidine and taurultam to treat cancer.

In response, Applicants respectfully traverse the rejections under 35 U.S.C. §103(a). As noted above, Applicants have described and shown an unexpected synergistic effect of the combination of 5-FU and a methylol transfer agent in the treatment of cancer. The Office Action has not set forth any technical reason to doubt this synergistic effect. Moreover, the Office Action has noted no suggestion in the cited art that a synergistic effect, such as that reflected in Applicants' claims, would result or be expected upon the combination of 5-FU and a methylol transfer agent. Accordingly, Applicants' showing of an unexpected synergistic effect of the claimed combination renders the claims unobvious over any combination of the art cited in the Office Action. Applicants therefore respectfully request reconsideration and withdrawal of the rejection of claims 1-11 under 35 U.S.C. §103.

Double Patenting rejection

Claims 1-11 were rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-2 of U.S. Patent No. 6,479,481, in view of the disclosure in '481. Although the conflicting claims are not identical, the Office Action asserted that they are not patentably distinct from each other because the '481 patent discloses a method of treating tumors using the methylol transfer agents taurolidine, taurultam or a mixture thereof, and teaches that it may be combined with 5-FU to treat glioblastoma (column 9, lines 13-43).

In response, Applicants would be willing to file a Terminal Disclaimer should any conflicting claims be found allowable.

Information Disclosure Statement

According to the Office Action, Monson (10), Monson (11) and Weberchock were not received and therefore could not be considered.

In response, Applicants point out that the two Monson references were cited by or submitted to the Office in U.S. Pat. No. 6,479,481, to which the present application claims priority under 35 U.S.C. §120 and thus, these references should be in the possession of the Office and are not required to be submitted. Applicants will forward a copy of the Weberchock reference to the Office shortly for consideration.

In view of the above remarks and claim amendments, Applicants believe that the Examiner's rejections set forth in the December 15, 2005 Office Action have been fully addressed and that the present claims fully satisfy the patent statutes. Applicants therefore believe that the application is in condition for allowance. The Examiner is invited to telephone the undersigned if it is deemed to expedite allowance of the application.

Respectfully submitted,

By: _____

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